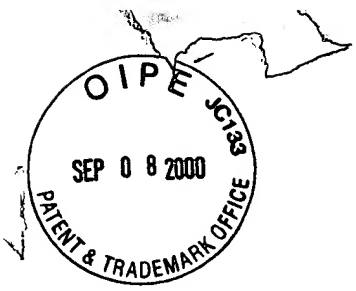


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R. PERRY MCCONNELL

ADMITTED TO PRACTICE:

UNITED STATES SUPREME COURT

UNITED STATES APPELLATE & DISTRICT COURTS

ALL TEXAS COURTS

UNITED STATES PATENT & TRADEMARK OFFICE

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September 8, 2000

Assistant Commissioner of Patents
Washington, D.C. 20231

re: Application No.: 09/358,103
Group Art Unit: 1652
Examiner: Christian L. Fonda
Atty. Docket: ROCA-01

Dear Sir:

Applicant's response to the Third Office Action is enclosed for filing, together with my firm check for the $55.00 one month extension fee.

Sincerely,

R. Perry McConnell
Reg. No. 38,239

enclosure

cc: Dr. Alberto Roca

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | |
|---|---|---|
| In re Application of: | § | Group Art Unit: 1652 |
| Alberto I. Roca | § | |
| | § | |
| Serial No.: 09/358,103 | § | |
| | § | Examiner: Christian L. Fonda |
| Filed: July 21, 1999 | § | |
| | § | |
| For: Mutants of MAW Motifs of RecA | § | |
| Protein Homologs, Methods of | § | |
| Making Them, and Their Uses | § | Atty. Docket: ROCA-01 |

## RESPONSE TO THIRD OFFICE ACTION

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Dear Sir:

In response to the Office Action dated May 10, 2000:

Notice of Change of Address of Counsel

Please note that counsel's mailing address has changed. The new address is:

Perry McConnell
R. Perry McConnell, P.C.
9001 Forest Crossing, Suite F
The Woodlands, TX 77381

Counsel's telephone and facsimile numbers remain the same as before.

Petition for Extension of Time to Respond

Applicant respectfully petitions for a one-month extension of time to respond to the First Office Action, and encloses the requisite fee for such extension with this Response, pursuant to 37 C.F.R. §§ 1.136(a) and 1.17.

## Objections to the Drawings

Applicant acknowledges the required alteration to the margin of Figure 3, and requests that the examiner treat this as an informal drawing for the purpose of examination. Applicant will submit a final drawing for Figure 3 which conforms to Patent and Trademark Office requirements when required by the Examiner.

## The Rejection Under 35 U.S.C. § 112

Claim 1 was rejected under 35 U.S.C. § 112, second paragraph on the basis that the phrase "In an *E.coli* RecA protein or a protein having a MAW motif homologous to the *E. coli* MAW motif, a RecA homolog protein mutant" is indefinite. As stated in the specification, the term "RecA homolog protein" is defined as "an *E. coli* RecA protein having the MAW sequence at residues 40-65, inclusive, as shown in SEQ ID NO: 1, or a homolog thereof." (Application at p. 5, l. 22 - p. 6, l. 2). Therefore, a "RecA homolog protein mutant" is defined as a mutant of an *E. coli* RecA protein having the MAW motif, or a mutant of a homolog of such a protein.

Such homologs are understood by those skilled in the art to contain sequences homologous to the *E. coli* RecA MAW motif, although the homologous sequence may be displaced from positions 40-65, and the homologous sequence may contain residues varying from those of the MAW sequence of the *E. coli* RecA protein. *See, Story, et al.* (1993) at 1893 (discussing structures which establish homology between DMC1, UvsX, and bacterial RecA proteins); *see also*, Fig. 1 of the application and the discussion thereof at page 8, *et seq.* of the application. Thus, those of skill in the art understand the concept of homology between proteins, and will understand from the description what is meant by a mutant of a RecA homolog protein. That this description suffices to define the invention is further underscored by the Examiner's selection of four naturally-occurring RecA homolog proteins

(Alignments 1-4), even though the MAW-motif homologs did not occur in those examples at sequence positions 40-65. Accordingly, those of skill in the art will understand what is meant by a "RecA homolog protein," and therefore will also understand the meaning of "RecA homolog protein mutant." Applicant respectfully submits that the Examiner's rejection on this basis is incorrect.

The examiner also rejected claims 1-27 as indefinite because the claims reference positions such as 42, 52, and 53, which do not appear in SEQ ID NO:1, which consists of twenty-six residues. However, the comments to SEQ ID NO:1 establish that the listed sequence is the MAW motif, that positions 1 and 26 are not terminal, and that the listed sequence corresponds to positions 40-65 of the RecA protein. Accordingly, those of skill in the art will understand that position 1 of SEQ ID NO:1 corresponds to position 40 of the RecA protein and the first position of the MAW motif in its homologs. Further, the claims do not assert simply "residue 42," etc. but refer to positions which are homologs of that position in *E. coli* RecA. Again, the Examiner's own selection of four naturally-occurring RecA homologs in which the MAW motif does not occur at either positions 1-26 *or* 40-65 underscores that those of skill in the art will understand this description and will recognize that position 1 of SEQ ID NO:1 corresponds to residue 40 of *E. coli* RecA, and to the first position of the MAW motif in a RecA homolog. Accordingly, Applicant respectfully submits that the Examiner's rejection is incorrect, and that claims 1-27 are not indefinite.

The Rejections Under 35 U.S.C. § 101 and 35 U.S.C. § 112, First Paragraph

The examiner has rejected claims 1-27 under 35 U.S.C. § 101, predicated on the conclusion that the invention does not have either a credible asserted utility or a well established utility. However, "[t]o violate section 101, the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992). Thus,

To be "useful," it is not necessary for a patented device to meet *every* objective stated in the specification; rather, "[w]hen a properly claimed invention meets at least one stated objective, utility under § 101 is clearly shown." *Carl Zeiss Stiftung v. Renishaw plc*, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991), *quoting Raytheon Co. v. Roper Corp.*, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983), *cert. denied* 469 U.S. 835 (1984).

Among the Examiner's objections were the absence of working examples comparing wild type RecA and mutant proteins in the presence or absence of ATPγS. However, as discussed in Example 2, a mutant of this invention has exhibited increased activity in the absence of ATPγS. *See*, Example 2 & Fig. 2. Therefore, the specification is affirmatively supported by working example that the invention demonstrates heightened activity absent the cofactor. Because at least one stated objective is established, "utility under § 101 is clearly shown." *Carl Zeiss Stiftung*, at *Id.*

Accordingly, Applicant respectfully submits that the invention has disclosed has at least a credible asserted utility, and that the rejection under section 101 is incorrect.

The examiner has also rejected claims 1-27 under 35 U.S.C. § 112, first paragraph, predicated solely on the examiner's conclusion that the invention has no utility. Because, as discussed above, the rejection under 35 U.S.C. § 101 is incorrect, the rejection under section 112 is also incorrect. Further, the Examiner's conclusion that those of skill in the art "clearly would not know how to use the claimed invention" is negated by the Examiner's own later statement (concerning the section 103 rejection) that "one of ordinary skill in the art would be motivated to make RecA mutants or homologs of RecA mutants with enhanced properties for use in homologous recombination based gene therapies." It stands to reason that one of skill in the art would not be motivated to make something which he had no idea how to use. One of skill in the art would, as the Examiner has recognized, clearly understand

how to use the present invention, *e.g.* by substituting this invention for wild-type RecA in situations in which the wild-type RecA's properties must otherwise be artificially enhanced. Accordingly, Applicant respectfully submits that claims 1-27 are in condition for allowance under 35 U.S.C. §§ 102 and 112, first paragraph.

The Rejections Under 35 U.S.C. § 102

1. Rejection of claims 1, 2, 8, and 9

The examiner has rejected claims 1, 2, 8, and 9 as being anticipated by *Zarling, et al.* (**Alignment 1**). This rejection is based on the existence of an arginine residue, rather than a glycine residue, at position 43 of an *E. coli* MAW motif homolog. However, **Alignment 1** reflects a naturally-occurring MAW-motif sequence in a non-*E. coli* RecA protein. (**Alignment 1**).

Claim 1 recites:

". . .a RecA homolog protein *mutant*, *wherein a naturally occurring amino acid residue* located within the protein's homolog of *E. coli* residues 40 to 65, inclusive, shown in SEQ ID NO: 1, *is replaced* with a replacement amino acid residue which is volumetrically larger than the replaced amino acid residue." (emphasis added). Claim 2 depends from claim 1, and claims 8 and 9 depend from claims 1 and 2, respectively.

A claim can only be anticipated if every element of the claim is explicitly or inherently recited in a single prior art reference. MPEP 706.02. **Alignment 1** neither explicitly nor inherently teaches either a *mutant* or *replacement* of a naturally-occurring residue with any other residue. Rather, it simply recites a naturally-occurring sequence. Accordingly, **Alignment 1** does not reflect every element of claims 1, 2, 8, or 9, and Applicant respectfully submits that none of these claims is anticipated by **Alignment 1**.

2. Rejection of claims 4, 15, and 21

The examiner has rejected claims 4, 15, and 21 as being anticipated by *Garcia.* (**Alignment 2**). This rejection is based on the existence of an isoleucine residue at position 53, and a phenylalanine residue at position 60, of an *E. coli* MAW motif homolog. However, **Alignment 2** reflects a naturally-occurring MAW-motif sequence in a non-*E. coli* RecA protein. (**Alignment 2**).

Claim 4 depends from Claim 1. Claim 1 recites:

". . .a RecA homolog protein *mutant*, *wherein a naturally occurring amino acid residue* located within the protein's homolog of *E. coli* residues 40 to 65, inclusive, shown in SEQ ID NO: 1, *is replaced* with a replacement amino acid residue which is volumetrically larger than the replaced amino acid residue." (emphasis added).

Claim 15 recites:

". . . a RecA homolog protein *mutant*, wherein a naturally occurring amino acid residue located within the protein's homolog of *E. coli* residues 40 to 65, shown in SEQ ID NO: 1, inclusive, but excluding residues 47 and 51, *is replaced* with a replacement aromatic amino acid residue." (emphasis added). Claim 21 depends from claim 15.

A claim can only be anticipated if every element of the claim is explicitly or inherently recited in a single prior art reference. MPEP 706.02. **Alignment 2** neither explicitly nor inherently teaches either a *mutant* or *replacement* of a naturally-occurring residue with any other residue. Rather, it simply recites a naturally-occurring sequence. Accordingly, **Alignment 2** does not reflect every element of claims 4, 15, or 21, and Applicant respectfully submits that none of these claims is anticipated by **Alignment 2**.

3. Rejection of claims 7 and 14

The examiner has rejected claims 7 and 14 as being anticipated by *McKean, et al.* (**Alignment 3**). This rejection is based on the existence of arginine residue at position 59 of an *E. coli* MAW motif homolog. However, **Alignment 3** reflects a naturally-occurring MAW-motif sequence in a non-*E. coli* RecA protein. (**Alignment 3**).

Claim 7 depends from Claim 1, and Claim 14 depends from Claim 7. Claim 1 recites:

". . .a RecA homolog protein *mutant*, *wherein a naturally occurring amino acid residue* located within the protein's homolog of *E. coli* residues 40 to 65, inclusive, shown in SEQ ID NO: 1, *is replaced* with a replacement amino acid residue which is volumetrically larger than the replaced amino acid residue." (emphasis added).

A claim can only be anticipated if every element of the claim is explicitly or inherently recited in a single prior art reference. MPEP 706.02. **Alignment 3** neither explicitly nor inherently teaches either a *mutant* or *replacement* of a naturally-occurring residue with any other residue. Rather, it simply recites a naturally-occurring sequence. Accordingly, **Alignment 3** does not reflect every element of claims 7 and 14, and Applicant respectfully submits that neither of these claims is anticipated by **Alignment 1**.

4. Rejection of claims 16 and 22

The examiner has rejected claims 16 and 22 as being anticipated by *Ramesar, et al.* (**Alignment 4**). This rejection is based on the existence of a tryptophan residue at the homolog to position 40 of an *E. coli* MAW motif homolog. This rejection is misplaced, because **Alignment 4** discloses a *tyrosine*, not a *tryptophan* residue Further, **Alignment 4** reflects a naturally-occurring MAW-motif sequence in a non-*E. coli* RecA protein. (**Alignment 4**).

Claim 16 depends from Claim 15, and Claim 22 depends from Claim 16. Claim 15 recites:

". . . a RecA homolog protein *mutant*, wherein a naturally occurring amino acid residue located within the protein's homolog of *E. coli* residues 40 to 65, shown in SEQ ID NO: 1, inclusive, but excluding residues 47 and 51, *is replaced* with a replacement aromatic amino acid residue." (emphasis added).

A claim can only be anticipated if every element of the claim is explicitly or inherently recited in a single prior art reference. MPEP 706.02. **Alignment 4** neither explicitly nor inherently teaches either a *mutant* or *replacement* of a naturally-occurring residue with any other residue. Rather, it simply recites a naturally-occurring sequence. Accordingly, **Alignment 4** does not reflect every element of claims 16 or 22, and Applicant respectfully submits that neither of these claims is anticipated by **Alignment 4**.

The Rejections Under 35 U.S.C. § 103

In the Office Action, claims 1-27 were rejected under 35 U.S.C. § 103 as being unpatentable over *Konola, et al.* in view of *Story, et al.* (1993), *Story, et al.* (1992), and *Menetski, et al.* Applicant submits that these claims are not obviated by any of the cited prior art references, either singularly or in combination.

To establish a *prima facie* case of obviousness, three criteria must be met:

(1) There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings;

(2) There must be a reasonable expectation of success; and

(3) The prior art references must teach or suggest all of the claim limitations.

Additionally, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991); See, also, MPEP # 706.02(j). Reading *Konola, et al., Story, et al.* (1993), *Story, et al.* (1992), and *Menetski, et al.* together does not meet these criteria.

In the Examiner's analysis, steps A-E are suggested as being obvious steps in view of the four cited references. Within Step A, the Examiner states that "*Story, et al.* (1993) teach[es] class IV residues which are part of the MAW motif," and that it would be possible to "modify amino acid residues in the MAW motif of the RecA protein [as] taught by *Konola, et al.*" However, *Story, et al.* (1993) teaches away from the present invention, because *Story, et al.* (1993) argues that the ATP binding site is "distant" from the MAW motif. *See, Story, et al.* (1993) at 1893 and Table 1, p. 1894. Not only is there no suggestion in the cited references to combine these references to create the present invention, but the references themselves teach away from it.

Further, the Examiner's reference to modification of "amino acid residues in the MAW motif of the RecA protein [as] taught by *Konola, et al.* is confusing, because *Konola* does not teach modification of residues within the MAW motif, but rather in the P-loop (residues 66-75). *Konola, et al.*

Accordingly, the *In re Vaeck* criteria are not met for the following reasons:

Criterion #1: <u>There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings</u>

There is no suggestion or motivation in the prior art cited or in general knowledge, to combine the cited references in such a way as to produce the present invention. As mentioned above, *Story, et*

*al.* (1993) teaches away from the concept that the MAW motif is involved in ATP-binding at all. Further, none of the references cited suggest that single-site residue modifications to RecA MAW motif homologs would change "the conformation of the RecA protein or homolog in the same manner ATP induces a conformational change."

The Examiner's suggestion in Step A that "[m]odification of amino acid residues include substitution with amino acid residues that are volumetrically larger than the wild type amino acid residues or substitution with aromatic amino acid residues or conservative substitutions" is unsupported by any prior art reference. None of the references cited provide any motivation to perform such substitutions within homologs of the MAW motif, nor do the prior art references disclose the particular types of substitutions of the present invention. Accordingly, criterion number one is not satisfied.

Criterion #2: There must be a reasonable expectation of success

As discussed above, the cited prior art suggests that the MAW motif is "distant from the ATP-binding site." *Story, et al.* (1993). Accordingly, based on the cited prior art, there would be no expectation of success of the present invention.

Criterion #3: The prior art references must teach or suggest all of the claim limitations

The cited prior art does not teach or suggest all of the claim limitations. The Examiner's recitation of Steps A-E can encompass the present invention only by the insertion of the statement that "[m]odification of amino acid residues include substitution with amino acid residues that are volumetrically larger than the wild type amino acid residues or substitution with aromatic amino acid residues or conservative substitutions." This statement is unsupported by any cited prior art reference and cannot support an obviousness rejection.

Because the criteria to establish a *prima facie* obviousness rejection are not satisfied in this case, Applicant respectfully submits that claims 1-27 are not obvious in view of the prior art.

Conclusion

Applicant respectfully submits that claims 1-27 are in condition for allowance and requests that the Examiner issue a Notice of Allowance of these claims.

Respectfully submitted,

Date: 9/8/00

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CERTIFICATE OF MAILING VIA EXPRESS MAIL UNDER 37 C.F.R. § 1.10

I hereby certify that the above **Response to Third Office Action** is being mailed to the Assistant Commissioner of Patents, Washington, D.C. 20231, via the United States Postal Service Express Mail, on the 8th day of September, 2000.

Express Mail No.: EK694559923US